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Indium Metal as a Reducing Agent. Selective Reduction of the Carbon–Carbon Double Bond in Highly Activated Conjugated Alkenes

Brindaban C. Ranu,* Jyotirmoy Dutta, and Sankar K. Guchhait

Department of Organic Chemistry, Indian Association for the Cultivation of Science,
Jadavpur, Calcutta 700 032, India

ocbcr@mahendra.iacs.res.in

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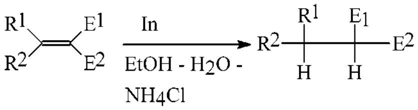
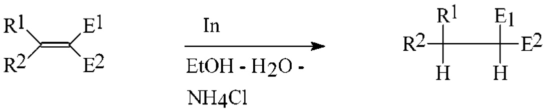
ABSTRACT



Indium metal in aqueous ethanolic ammonium chloride reduces the C═C bond in highly activated conjugated alkenes such as α,α-dicyano olefins, *β*-arylenones, and enone esters.

In recent times, indium metal has been the subject of current interest because of its high potential in organic synthesis.[1] However, although indium has been used extensively in the generation of synthetically useful allylindium species,[1,2] its use in other domains has not been explored to any great extent. Because of the close resemblance of indium to magnesium and zinc in several respects including first ionization potential, we envisioned indium to be a potential reducing agent and initiated a systematic investigation into reduction by indium metal. Surprisingly, reduction by indium is virtually unexplored except for a number of recent examples,[3] which include reduction of nitro groups,[3a] the heterocyclic ring in quinolines,[3b] azides,[3c] and *N*-oxides[3f] among others. On the other hand, our efforts during these years achieved stereoselective reduction of aryl-substituted *vic*- and *gem*-dibromides,[4a,4b] reductive dehalogenation of α-halocarbonyl compounds and benzyl halides,[4c] and reduction of terminal alkynes to alkenes.[4d] Although, in general, organoindium reagents and indium metal are known to be relatively inert toward isolated carbon−carbon double bonds,[1−4] no detailed and systematic investigation has been carried out to look into various activated systems. So, as a part of our continuing program[4] we have discovered that indium in aqueous ethanolic ammonium chloride reduces carbon−carbon double bonds in highly activated conjugated alkenes (Scheme 1).

Scheme 1



Subsequently, a very recent report by Moody et al.[5] shows reduction of C═C bond in three α,*β*-unsaturated ketones by indium in THF in the presence of acetic acid.

In a typical general experimental procedure,[6] an alkene was heated under reflux with indium in aqueous ethanolic

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(1) (a) Li, C.-J. *Chem. Rev.* **1993**, *93*, 2023. (b) Cintas, P. *Synlett* **1995**, 1087. (c) Li, C.-J. *Tetrahedron* **1996**, *52*, 5643. (d) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149. (e) Chauhan, K. K.; Frost, C. G. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3015. (f) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347.

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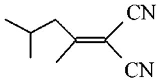
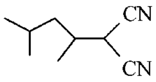
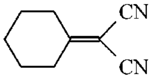
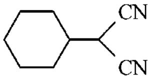
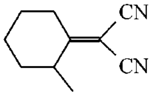
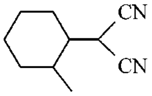
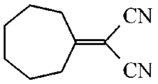
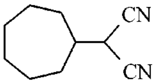
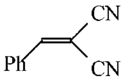
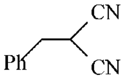
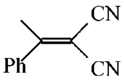
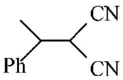
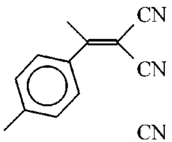
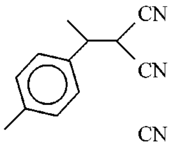
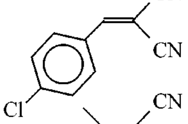
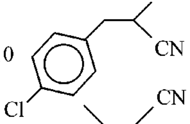
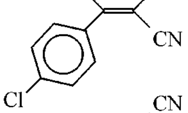
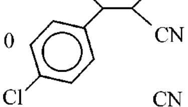
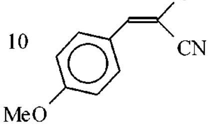
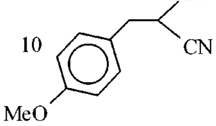
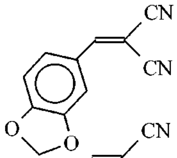
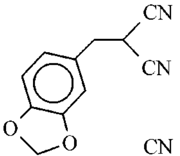
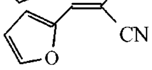
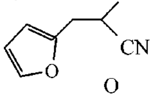
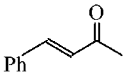
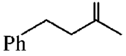
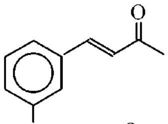
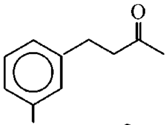
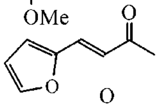
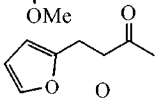
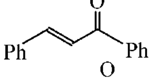
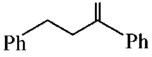
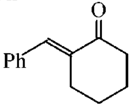
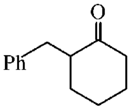
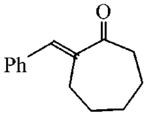
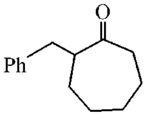
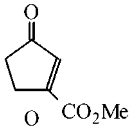
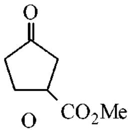
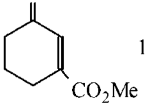
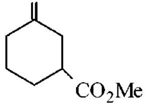
Table 1. Reduction of Conjugated Alkenes by Indium Metal

entry	alkene	time(h)	product	yield(%)[a]	ref.
1		9		80	
2		9		85	7
3		10		83[b]	
4		10		90	7
5		9		86	
6		10		80	
7		10		80	
8		10		82	8
9		10		80	
10		10		80	8
11		10		80	
12		2		58	9
13		12		40	5
14		12		70	10
15		10		75	11
16		12		30	5
17		13		70	12
18		30		55	13
19		14		65	14
20		13		70	14

[a] Yields refer to those of purified isolated products fully characterized by spectral and analytical data. [b] As mixture of diastereomers in 4:1 ratio.

ammonium chloride solution (mixed in a definite proportion) for a certain period of time as required to complete the reaction. Extraction with ether and usual workup provided the corresponding reduced product.

A wide range of structurally varied highly activated (electron-deficient) alkenes underwent selective reductions of the C=C bonds by this procedure to provide the corresponding alkanes. The substrates include α,α-dicyano alkenes, β-aryl-substituted enones, and conjugated enone esters. The results are presented in Table 1. As evident from the table, while the reduction of dicyano alkenes are considerably clean, those of conjugated enones and enone esters are not always satisfactory and are rather tricky. Thus, benzylideneacetone (entry 13) and chalcone (entry 16) furnished poor yields, producing other undesirable side products. A similar problem was also reported by Moody et al.[5] in the reduction of chalcone by their procedure. It has

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been found that reduction of $\mathrm{C{=}C}$ bond depends significantly on the electron deficiency of alkene, and thus, relatively less electron-deficient $\mathrm{C{=}C}$ bonds in α,α-dicarboalkoxy alkenes and α-cyano, α-carboalkoxy olefins did not undergo reduction at all. On the other hand, substitution on the aromatic ring of the β-aryl moiety also greatly influences the reduction. Thus, *m*-methoxy phenyl enone (entry 14) underwent smooth reduction, whereas the corresponding *o*-and *p*-methoxy phenyl analogues failed to go for such reduction.

In general, the reductions by this procedure are clean, high-yielding, and reasonably fast. The reaction conditions are mild enough to tolerate acid-sensitive functionalities such as methoxy (entries 10,14), methylenedioxy (entry 11), and carboxylic ester (entries 19 and 20). This reagent is also highly chemoselective, reducing only the electron-deficient $\mathrm{C{=}C}$ bond without affecting several easily reducible functional groups such as $-\mathrm{C{\equiv}N}$, $-\mathrm{C{=}O}$, and $-\mathrm{CO_2R}$.

To conclude, the present procedure using indium metal in aqueous ethanolic ammonium chloride provides a chemoselective reduction of the $\mathrm{C{=}C}$ bond in highly activated alkenes. The notable advantages of this procedure are as follows: (a) operational simplicity, (b) exclusive compatibility with several acid-sensitive and easily reducible functionalities, (c) good yields, and (d) green chemistry. Moreover, this study constitutes a systematic investigation of the reduction of a $\mathrm{C{=}C}$ bond with scopes and limitations by indium metal, and certainly it broadens the perview of further research in this area.

Acknowledgment. This investigation has enjoyed financial support from the CSIR, New Delhi. J.D is thankful to CSIR for his fellowship.

Supporting Information Available: Spectral and analytical data for all reduced products (alkanes), not reported earlier, designated by their entries in Table 1.

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(6) **General Experimental Procedure**. 1,1-Dicyano-2-phenyl ethylene (entry 5) (154 mg, 1 mmol) was heated under reflux at an oil bath temperature of 90 °C with indium (173 mg, 1.5 mmol) (commercially available ingot from SRL, India, cut into small pieces) in aqueous ethanolic ammonium chloride solution (1.5 mL of EtOH, 1.5 mL of H_2O, 1 g of NH_4Cl) for 9 h (TLC). Ethanol was removed under vacuum, and the residue was extracted with ether. The extract was washed with brine, dried (Na_2SO_4), and evaporated to leave the crude product, which was purified by column chromatography over silica gel (eluting solvent system, hexanes−ether in 98:2 ratio) to furnish the corresponding alkane (135 mg, 86%) as a white solid, mp 87 °C: IR 2255 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.29 (2H, d, $J = 6.9$ Hz), 3.91 (1H, t, $J = 6.9$ Hz), 7.26−7.47 (5H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.0, 36.8, 112.1(2), 128.8, 129.1(2), 129.3(2), 132.9. Anal. Calcd for $C_{10}H_8N_2$: C, 76.90; H, 5.16. Found: C, 76.59; H, 5.05. This procedure has been followed for the reduction of all conjugated alkenes listed in Table 1. The compounds have been characterized by their physical and spectral (IR, ^1H NMR and ^{13}C NMR) data in comparison with the reported values whenever available and by elemental analysis.

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